UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,704	05/16/2002	Camilo Anthony Leo Selwyn Colaco	8830-21	7595

7590 09/18/2009

Drinker Biddle & Reath
One Logan Square
18th & Cherry Streets
Philadelphia, PA 19103-6996

EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
09/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/049,704	COLACO, CAMILO ANTHONY LEO SELWYN	
	Examiner	Art Unit	
	GINNY PORTNER	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 17* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-14 and 17* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/15/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-15, 17 are pending. Claims 10-14 and 17 are under consideration; claims 1-9, 15 stand withdrawn from consideration.

Information Disclosure Statement

1. The information disclosure statement filed June 15, 2009 has been considered.

Rejections Withdrawn

2. ***Withdrawn, Claim Rejections - 35 USC § 102***: The rejection of claims 10-14, and claim 17 under 35 U.S.C. 102(e) as being anticipated by Srivastava (US 5,961,979) is herein withdrawn in light of the amendment of all of the claims to be directed to heat shock protein complexes from extracellular bacterial pathogens.

3. ***Withdrawn,*** The rejection of claim 10 under 35 U.S.C. 102(a) as being anticipated by Motohashi et al (June 1999), is herein withdrawn in light of the amendment of all of the claims to be directed to heat shock protein complexes from extracellular bacterial pathogens.

4. ***Withdrawn***, The rejection of claims 10-14 and 17 under 35 U.S.C. 102(e) as being anticipated by Langermann et al (US Pat. 6,500,434, claims 1-33) is herein withdrawn in light of FimC/FimH do not associate in an ATP dependent manner, though the complex is the combination of an heat shock protein and a peptide, which are induced in vivo selectively, this complex does not meet the functional limitations of the recited process "ATP-dependent reaction", even though ATP is not present in the claimed composition.

Response to Arguments for Rejections Maintained

5. Applicant's arguments filed June 15, 2009 have been fully considered but they are not persuasive.

Double Patenting

1. ***Maintained:*** Claims 10, 12 and 17 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, and 12 of copending Application No. 10/363,454 is herein maintained as an effective terminal disclaimer was not submitted. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. ***Maintained***, The rejection of claims 10-11, 17 rejected under 35 U.S.C. 102(b) as being anticipated by Phipps et al (1991) is traversed on the grounds that the Phipps et al complex is obtained from Pyrodictium occultum which is not an extra-cellular pathogen, that the complex is enriched and not induced by heat shock and therefore does not teach the claimed product based upon the process limitation recited in the claims.

3. Applicant's traversal with respect to Phipps is partially convincing (rejection withdrawn over claims 13-14), in so far as the Remarks and traversal are directed to Pyrodictium occultum in light of the amendment of the claims to recite "extracellular pathogenic bacteria", but it is the position of the examiner that Phipps et al still discloses a composition that comprises a heat shock protein/peptide complex produced in-situ (in

the natural host) by extracting the complex from an extra-cellular pathogenic bacteria, namely E. coli (see Phipps, page 1716 col. 2, last paragraph).

4. Phipps et al teach the isolation of the heat shock protein/peptide complexes produced by E.coli following heat shock (see page 1716, col. 2, last paragraph) based upon French press cell lysis/extracton ("Membrane-free French press lysates of several archae bacteria, the eubacteria E.coli (Also see page 1717, Figure 10, lane h. "Escherichia coli"; page 1717, col. 2, p. 2).

5. Traversal directed to increased constitutive expression, is being viewed by the examiner as being another way of saying induced higher levels of a constitutive protein (The E.coli complex was produced by heat shock which resulted in an induced/elevated synthesis of heat shock proteins: "The complex is preferentially accumulated following heat shock"; the "Living organisms including archaebacteria respond to an upshift in temperature by elevating the synthesis of a defined set of cellular proteins, known as heat shock proteins and accumulating them to higher steady state levels" (see page 1716, col. 2, last paragraph).

6. Traversal directed to inducible verses constitutive gene expression is not convincing because Applicant's Specification teaches the production of the claimed composition based upon constitutive expression in a genetically engineered bacteria without the need to apply external stresses (see Instant Specification page 7, p. 4), therefore Applicant's claims encompasses heat/stress protein/peptide complexes that may be produced by induction or constitutive expression, as long as the complex comprises the required products that include a heat shock protein complexed with a peptide and are endogenous to an extracellular pathogenic bacteria.

7. Phipps et al clearly teaches the induction of "A novel ATPase complex selectively accumulated upon heat shock (title)" and a similar process of induction (see page 1716, col. 2, last paragraph) was carried out with E.coli for evaluation of heat shock complexes

based upon immunological cross-reactivity assay (see Figure 10, lane h); E.coli being a known human extracelluar pathogen.

8. No specific proteins of any specific relative molecular weight or structure are required by the instant claims, therefore the heat shock protein/peptide complex of E.coli contained in the composition obtained by and resulting in a membrane free French press lysate anticipates the instantly claimed invention as now claimed. The disclosure of Phipps et al still meets the requirements of the claims directed to compositions that comprise a heat shock protein/peptide complex produced by a heat shock stimulus, the complex is accomplished in an ATP dependent manner and is accomplished in an ATP-dependent reaction (see title "ATPase complex"; fig 9-10). The purification or production of a product by a particular process (i.e. the instant recombinant) does not impart novelty or unobviousness to a product when the product is taught by the prior art. This is particularly true, when the properties of the product are not changed by the process in an unexpected manner. *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); and *In re Brown*, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught by the prior art. *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 559, 601, 38 USPQ 143-45 (CCPA 1938); and *United States v. Ciba-Geigy Corp.*, 508 F.supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

1. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a

novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

9. The rejection of claims 10-11 rejected under 35 U.S.C. 102(b) as being anticipated by Wawrzynow et al (1995) is traversed on the grounds that the heat shock protein complex of Wawrzynow et al is not produced under heat shock in the experiments of Wawrzynow, but rather at steady state conditions of 37°C, and points to Exhibit 4 for the method of purification of the individual components of the ClpP-ClpX complex of Wawrzynow et al (1995, applied reference)

10. Upon consideration of Applicant's traversal and Exhibit 4 which was provided as evidence that Wawrzynow et al did not obtain the heat shock protein/peptide complex based upon a temperature heat shock/purification process, it is the position of the examiner that the process by which the claimed complex is produced is not critical as long as the product is the same or equivalent product produced by a different process. The heat shock protein (ClpX) is described as a protein that is "under heat-shock regulation (see Wawrzynow et al page 1868, col. 1, last two lines)" and λO peptide is a peptide found within E.coli strains carrying bacteriophage (see abstract) sequences.

11. Wawrzynow et al teach ClpX is a heat shock protein of Escherichia coli (see title, abstract), and is an ATP-dependent substrate specificity component of the ClpP-ClpX protease (see title, abstract), that also functions as a chaperone for λO (see page 1867, col. 2, p. 3). "λO activity was protected by the addition of the ClpX protein and ATP during

the preincubation treatment" through the formation of a ClpX- λO peptide complex. "λO protein is heat labile at 30°C", but was protected when ClpX was added at nanomolar concentrations to the λO protein solution at 30°C (page 1867, col. 2, p. 3, bottom of paragraph). The ClpX heat shock protein-λO peptide complex of Wawrzynow et al was produced by a different process, but is the same or equivalent heat shock protein/ peptide complex as now claimed, the complex being an endogenous complex found to Ecoli, and is a heat shock protein complex of an extracellular pathogenic bacteria, the formation of the complex being ATP dependent.

Wawrzynow et al is maintained for reasons of record and responses set forth herein.

New Grounds of Objection/Rejection

Objections

12. Claim 13 is objected to because of the following informalities: Claim 13 recites the phrase "comprises and aqueous carrier"; this should be ---comprises an aqueous carrier----.

13. The disclosure is objected to because of the following informalities: At page 7 line 18 of the Specification, "Trypanosoma sp.." is described to be a bacteria, but is a parasite, not a bacteria.

```
may be applied include bacteria such as Mycobacteria sp.,
notably M Bovis and M Tuberculosis, Helicobacter sp.,
Streptococcus sp., Trypanosoma sp., Mycoplasma sp.; and
```

Appropriate correction is required.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 10, 11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Laminet et al (EMBO Journal, 1990, vol. 9(7), pages 2315-139, reference of record, being reinstated in light of claim amendment(s)).

Please Note: The following art rejection is being reinstated in light of the fact that all of the claims have been amended to recite the term **"extracellular pathogenic bacteria"**

Instant claims 10-11: Laminet et al disclose a composition that comprises an isolated E.coli heat shock protein complex GroEL/ES (see abstract and page 2317, col. 1, p. 2, middle of paragraph).

Instant claim 13: The composition comprises an aqueous carrier as the component parts of the composition contained Mg^{2+} and ATP present at a final concentration of 5 mM. (see Figure 3, narrative for frame (A)).

16. Applicant has defined E.coli as an extracelluar pathogen in their Examples section and in the Specification, page 7, lines 19-20.

17. Laminet et al anticipates the instantly claimed invention as now claimed.

18. The purification or production of a product by a particular process (i.e. the instant recombinant) does not impart novelty or unobviousness to a product when the product is taught by the prior art. This is particularly true, when the properties of the product are

not changed by the process in an unexpected manner. *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); and *In re Brown*, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught by the prior art. *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 559, 601, 38 USPQ 143-45 (CCPA 1938); and *United States v. Ciba-Geigy Corp.*, 508 F.supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

19. Claims 10-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ferrero et al (1995, reference of record.) in light of evidence provided by Schumann (2000)

Please Note: This rejection is being reinstated in light of Applicant claim amendment to recite "extracellular pathogenic bacteria".

Ferrero et al disclose the instantly claimed invention directed to :

Instant claims 10-11: composition that comprises a heat shock protein complex of

- HspA together with a peptide (urease (see page 6499, col. 2, p. 2 "The physical association between H. pylori HSP and urease") or
- GroES-GroEL H. pylori proteins referred to as HspA and HspB, respectively (abstract, Figure 1, "whole cell extracts" containing HSP homologs reacted with "hyperimmune rabbit antisera raised against H. pylori …HspA and … HspB")

Instant claim 12: the compositions further comprised an adjuvant

- Antigen extracts (50 ug of protein) containing 5 ug of cholera toxin" (a mucosal adjuvant)

Instant claim 13: together with an aqueous carrier ("were prepared in 0.1M sodium bicarbonate"(an aqueous carrier).

The heat shock proteins were expressed in situ and extracted from whole extracellular pathogenic bacteria (see page 6500, col. 1, Animal Experiments section H. felis).

Instant claim 14: Ferrero et al disclose a method of inducing an immune response in an animal ("mouse model") against infection by an extracellular pathogen (H. felis (mouse, cat and human pathogen) or H. pylori (mouse and human pathogen), the method comprising the step of:

Administering a pharmaceutically acceptable quantity (50 ug of antigen or 1 mg of whole cell sonicate, see Ledger for Table 2, page 6501) of a composition for inducing an immune response as claimed in claim 10 sufficient to elicit an immune response in the animal to said pathogenic bacteria (see Figure 2, page 6501, "serum antibodies" of HspA/UreB or HspA/HspB (whole cell extract/sonicate)) and Table 2, which shows 0/10 animal became infected).

Ferrero et al while not discussing the requirement for ATP in forming the HSP/peptide complex, but discloses the association of a Helicobacter heat shock protein and a peptide and therefore inherently anticipates the instantly claimed invention as now claimed, in light of evidence provided by Schumann that shows GroEL and GroES heat shock proteins to be ATP-dependent molecular chaperones (see Table 2, page 6) for associating with another peptide.

Conclusion

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert B Mondesi/
Supervisory Patent Examiner,
Art Unit 1645

/Ginny Portner/
Examiner, Art Unit 1645
September 15, 2009